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10/098,642	03/15/2002	Tiecheng A. Qiao	84027WFN	7342

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/098,642	QIAO ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2003 & 4 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 14 November 2003 in which the specification and claims 1-2, 5, 7, 20-21 and 23 were amended and further in response to papers filed 4 February 2004 in which terminal disclaimer was submitted. All of the amendments have been thoroughly reviewed and entered.

The previous objections and rejections under 35 U.S.C. 112, second paragraph in the Office Action dated 2 September 2003 are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(b) are withdrawn in view of applicant's comments regarding bright field illumination. The previous rejections under obviousness-type double patenting are withdrawn in view of the terminal disclaimer.

The previous rejections under 35 U.S.C. 103(a) are maintained. All of the arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Claims 1-25 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite for the recitation "fluorescently/chemiluminescently" because it is unclear whether the "/" is intended to mean "and", "or" or "and/or". It is suggested that Claim 7 be amended to clarify.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in view of Seul et al (U.S. Patent Application Publication No. 2003/0138842 A1 having priority to 60/300,025 filed 21 June 2001) .

Regarding Claim 1, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the

microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a fluorescently labeled target sequence (page 29, Table V) and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11). Walt et al further teach that their method requires permeability of the gelling agent (page 22, lines 20-22) which suggests that a portion of the microsphere must be exposed but they do not specifically teach a portion of the microsphere is exposed above the gelatin coating. However, Seul et al teach a similar method (¶ 18) wherein the microspheres are exposed above the gelatin coating thereby permitting a binding reaction between the binding agent on the microsphere and a target in solution (page 4, lines 3-6). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the microsphere exposure of Seul et al to the microspheres of Walt et al thereby exposing the microsphere for target binding as suggested by Walt et al (page 22, lines 20-22). One of ordinary skill in the art would have been motivated to expose the microspheres above the gelatin coating for the expected benefit of permitting target binding as taught by Seul et al (page 4, lines 3-6).

Regarding Claim 2, Walt et al disclose the method wherein each subpopulation has a unique optical signature (bar code) and a unique probe sequence (page 17, lines 15-19).

Regarding Claim 3, Walt et al disclose the method wherein the optical bar code is generated by two or more colorants i.e. each optical signature is comprises of a mixture of dyes (page 16, liens 25-28).

Regarding Claim 4, Walt et al disclose the method wherein the optical barcode is generated by a mixture of red, green and blue i.e. each optical signature is comprises of a mixture of dyes including red, green and blue dyes e.g. rhodamine, Malacite green, and Cascade Blue™ (page 16, line 25-page 17, line 2).

Regarding Claim 5, Walt et al disclose the method wherein at least one subpopulation has a luminescent property (i.e. fluorescence) and wherein detecting includes whole frame

imaging capture of a resulting luminescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 6, Walt et al disclose the method wherein said processing uses a pattern recognition algorithm to obtain the identification (page 32, line 5-page 35, line 12).

Regarding Claim 7, Walt et al disclose the method wherein at least one subpopulation has a fluorescent property and wherein detecting includes whole frame imaging capture of a resulting fluorescent image resulting from probe-target interaction to produce a first image, whole frame imaging capture of the microarray under bright field illumination to obtain microsphere signature image (background) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Regarding Claim 8, Walt et al disclose the method wherein the substrate is characterized by an absence of specific sites capable of interaction physically or chemically with the microspheres i.e. a planar substrate or within a tube (page 7, liens 14-20).

Regarding Claim 9, Walt et al disclose the method wherein the microspheres bear surface active sites which contain the nucleic acid probe (page 14, lines 20-30).

Regarding Claim 10, Walt et al disclose the method wherein the microspheres have a mean diameter of between 1 and 50 microns (page 9, lines 21-23).

Regarding Claim 11, Walt et al disclose the method wherein the microspheres have a mean diameter of between 3 and 30 microns (page 9, lines 21-23).

Regarding Claim 12, Walt et al disclose the method wherein the microspheres have a mean diameter of between 5 and 20 microns (page 9, lines 21-23).

Regarding Claim 13, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 100 and 1 million microspheres per cm^2 (page 6, lines 21-24).

Regarding Claim 14, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 1,000 and 200,000 microspheres per cm^2 (page 6, lines 26-28).

Regarding Claim 15, Walt et al disclose the method wherein the microspheres are immobilized at a concentration of between 10,000 and 100,00 microspheres per cm^2 (page 6, lines 21-28).

Regarding Claim 16, Walt et al disclose the method wherein the microspheres comprise a synthetic or natural polymeric material (page 9, lines 11-18).

Regarding Claim 17-18, Walt et al disclose the method wherein the microspheres comprise an amorphous polymer e.g. polystyrene (page 9, lines 11-18).

6. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (a) (WO 00/16101, published 23 March 2000) and Seul et al (U.S. Patent Application Publication No. 2003/0138842 A1 having priority to 60/300,025 filed 21 June 2001) as applied to Claim 1 and further in view of Walt et al (b) (U.S. Patent Application Publication No. 2002/0172716 A1, filed 25 October 2000).

Regarding Claim 19, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the

microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) but they do not teach the microsphere contains less than 30 percent crosslinking agent. However, Walt et al (b) teach microsphere composition whereby the amount of crosslinking agent determines microsphere pore size i.e. increasing amounts of crosslinking agents decreases pore size (¶ 7) and pores provide access to the hollow portion of the microsphere. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microspheres for entrapping dye of Walt et al (a) with a percent crosslinking agent which provides appropriate access to the hollow portion of the microsphere for dye entrapment as suggested by Walt et al (b) for the obvious benefit of entrapping the optical signature-specific dyes.

7. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) and Seul et al (U.S. Patent Application Publication No. 2003/0138842 A1 having priority to 60/300,025 filed 21 June 2001) as applied to Claim 1 and further in view of Chang et al (U.S. Patent No. 4,873,102, issued 10 October 1989).

Regarding Claim 20, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-

population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a target sequence and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) but they are silent regarding the polymerization method. However, emulsion polymerization preparation of microspheres was well known in the art at the time the claimed invention was made as taught by Change et al (Example 1, Column 6, lines 25-57) wherein the method provides microspheres of very narrow size range. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the emulsion polymerization of Change et al to the microspheres of Walt et al to thereby provide microspheres of a uniform size as taught by Chang et al (Column 6, lines 26-28) for the obvious benefits of providing consistent microsphere surface area for surface interaction and thereby controlling interaction uniformity.

8. Claims 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in view of Porter et al (U.S. Patent No. 6,146,899, filed 26 February 1999).

Regarding Claim 21, Walt et al disclose a method of identifying nucleic acid samples comprising providing a microarray including a substrate coated with a composition including a population of microspheres dispersed in a fluid containing a precursor to a gelling agent and immobilized at random positions on the substrate (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion,

polyacrylamide or polyHEMA, page 22, lines 9-22). Walt et al further teach at least one sub-population contains an optical barcode generated from a colorant (i.e. dye) associated with the microsphere (page 16, line 15-page 17, line 2). Walt et al further teach the microspheres include a nucleic acid probe (page 12, lines 8-10) and the method includes contacting the array with a fluorescently labeled target sequence (page 29, Table V) and detecting the color barcode of the subpopulation due to the target probe interaction (page 13, lines 12-35 and Claim 11) wherein at least one subpopulation has a luminescent property (i.e. fluorescence) and wherein detecting includes whole frame imaging capture of a resulting luminescent image resulting from probe-target interaction to produce a first image and obtain microsphere signature image (Fig. 8-9) to produce a first image and processing the first and second image to identify the nucleic acid (page 40, lines 1-15).

Walt et al further teach the method wherein the microspheres are on a planar support e.g. glass and illuminated using a confocal microscope (page 7, lines 14-17) but they do not further teach bright field illumination. However, it was bright field illumination coupled with confocal image collection was well known in the art at the time the claimed invention was made as taught by Porter et al who teach that bright field illumination facilitated focusing while minimizing photobleaching (Column 4, lines 57-62). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the confocal illumination of Walt et al with the additional bright field illumination taught by Porter et al for the expected benefit of focusing the image while minimizing photobleaching as taught by Porter et al (Column 4, lines 57-62).

Regarding Claim 22, Walt et al disclose the method wherein said processing uses a pattern recognition algorithm to obtain the identification (page 32, line 5-page 35, line 12).

Regarding Claim 23, Walt et al disclose the method wherein each subpopulation has a unique optical signature (bar code) and a unique probe sequence (page 17, lines 15-19).

Regarding Claim 24, Walt et al disclose the method wherein the optical bar code is generated by two or more colorants i.e. each optical signature is comprises of a mixture of dyes (page 16, liens 25-28).

Regarding Claim 25, Walt et al disclose the method wherein the optical barcode is generated by a mixture of red, green and blue i.e. each optical signature is comprises of a mixture of dyes including red, green and blue dyes e.g. rhodamine, Malacite green, and Cascade Blue™ (page 16, line 25-page 17, line 2).

Response to Arguments

9. Applicant argues that the film forming polymers of Walt would not undergo sol-gel transition as in the instant invention. The argument has been considered but is not found persuasive because the instant claims are drawn to microspheres immobilized in a coating containing a "gelling agent" or "precursor to a gelling agent". The instantly claimed "precursor" encompasses a very large and very diverse genus of agents. As stated above, Walt teaches a precursor to a gelling agent (i.e. the randomly mixed microspheres within a solution are dripped onto the substrate wherein upon evaporation of the solution, the solution holds them in place and wherein the solution comprises solution such as Nafion, polyacrylamide or polyHEMA, page 22, lines 9-22). The teaching of Walt et al is encompassed by the broadly claimed precursor to a gelling agent. Furthermore, the claims do not require a sol-gel transition agent or a method step of sol-gel transition. Therefore, the arguments are not commensurate in scope with the claims.

Applicant argues that Walt does not teach bright field illumination. The argument is deeded moot in view of the withdrawn rejection and new grounds for rejection.

Applicant argues that Seul discloses external electrical fields which are not needed in the instant method; Walt (b) disclose hollow microspheres which are not needed in the instant invention; and Chang discloses magnetic particles which are not used in the instant invention. Therefore, Applicant argues that the references teach away from the instant invention.

Applicant's argument has been considered but is not found persuasive because the open claim language "comprising" encompasses any additional elements not recited in the instant claims.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
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